Fresh Whole Blood Transfusion: A Controversial Military Practice

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The transfusion of fresh whole blood (FWB) for trauma-induced coagulopathy is unusual in civilian practice. However, US military physicians have used FWB in every combat operation since the practice was introduced in World War I and continue to do so during current military operations. We discuss our review of all blood products administered to US military casualties in Operation Iraqi Freedom (OIF) between March and December 2003. FWB transfusions were most frequent when demands for massive transfusions wiped out existing blood supplies. FWB patients had the highest blood product requirements; however, mortality did not differ significantly between FWB and non-FWB patients overall or for massively transfused patients. We review the current military practice of FWB transfusion in combat theaters and conclude that FWB transfusion is convenient, safe, and effective in certain military situations.

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Fresh whole blood (FWB) transfusions for traumatic hemorrhage and coagulopathy gradually fell out of favor in civilian hospitals as licensed blood components became widely available after World War II. Compared with blood components that can be processed, tested, freeze-dried, packaged, stored, shipped, and reconstituted, fresh whole blood was considered to be logistically impractical, wasteful, and unsafe. Military physicians, however, never lost sight of the known benefits of whole blood,[1–4] and the practice of FWB transfusion from combat hospitals in World War II[5–7] continues to this day. Military surgical teams utilize FWB by relying on a "walking blood bank" of soldier donors when blood requirements outpace supplies or when coagulopathic patients require blood products unavailable at their current echelon of care—two conditions that often coincide. During the first Gulf War, FWB was used to treat several coagulopathic patients when platelet supplies ran short. It became the major blood product used in Somalia when the supply of tested packed red blood cells (PRBC) was exhausted, and it was used to treat profoundly coagulopathic casualties in Bosnia and Kosovo, accounting for 12% and 13%, respectively,

of all red blood cells used.[8–10] More recently, FWB was used in 13% of all transfused patients in Operation Iraqi Freedom (OIF).

FWB IN OPERATION IRAQI FREEDOM

Information from the US Army Blood Program was gathered for the purpose of analysis of transfusion practices in OIF after approval from the Brooke Army Medical Center Institutional Review Board. During the first 10 months of OIF, between March and December 2003, a total of 2,349 units of blood products were transfused to 281 patients (Table 1). Thirty-six of 281 (13%) patients received FWB, with these patients having greater overall blood product transfusion requirements than those who did not receive FWB, receiving 29 ± 15 units of blood products compared with 5.3 ± 5.1 units ($p < 0.001$). FWB accounted for 23% of the total products transfused in these 36 patients. Patients receiving FWB were transfused 14.3 ± 7.5 units of packed red blood cells (PRBC), significantly more than the 4.8 ± 4.2 red cell units transfused in non-FWB patients ($p < 0.001$). The same was true for fresh frozen plasma (FFP), with 8.2 ± 5.2 units being given to the FWB group and 3.6 ± 2.6 units to the non-FWB group ($p < 0.001$). All 281 patients received at least one unit of PRBC, (range 1–35 units). Massive transfusion (defined as the transfusion of >10 units RBC inclusive of FWB) was required by 60 of 281 patients (21%). Twenty-six of the 36 FWB patients (72%) were massively transfused. Average blood product requirements in massively transfused FWB patients were more than twice those of massively transfused non-FWB patients: 33 ± 15 units versus 15 ± 6.1 units. Twice the proportion of FWB patients (88%) received FFP as non-FWB patients (44%).

Mortality data were unavailable for 15 patients, none of whom had received FWB. There were a total of 35 deaths among the 266 patients with known outcomes, for an overall mortality rate of 13%. Seven of the 36 FWB patients died (19%), which did not differ significantly from the 12% (28/230) mortality in the non-FWB group ($p = 0.44$). Mortality

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Table 1 Overall Use of Blood Products in US Casualties in Operation Iraqi Freedom

Product	Units	Percent of Total*	Patients	Units/Patient (Range)†
Packed red blood cells	1697	72	281	6.0 (1–35)
Fresh whole blood	242	10	36	6.7 (1–29)
Fresh frozen plasma	360	15	62	5.8 (1–21)
Platelet concentrate	35	1.5	6	5.8 (2–16)
Cryoprecipitate	15	0.6	1	15

* Total not equal to 100% due to rounding.
† Units per patient receiving that blood product.

rates did not differ significantly for massively transfused patients either: 19% (5/26) for FWB patients compared with 26% (8/31) for non-FWB patients ($p = 0.87$).

FWB EFFICACY

The acquired coagulopathy of trauma is responsible for a large percentage of early deaths in civilian trauma practice and is a major cause of battlefield mortality.[10–14] The risk of coagulopathy is proportional to injury severity, and coagulopathy is exacerbated by the "bloody vicious cycle" of hemorrhage leading to resuscitation, leading to hemodilution and hypothermia, leading to further hemorrhage.[14–17] The transfusion of large amounts of preserved red blood cells contributes to a dilutional coagulopathy which is primarily the result of thrombocytopenia and poor platelet function.[18–20] In addition, compared with fresh blood cells, stored platelets demonstrate decreased thrombotic function. This is primarily because of a decrease in expression of high-affinity thrombin receptors during platelet storage.[21] Clinically, FWB has been demonstrated to reverse dilutional coagulopathy, with evidence that a single unit of FWB has a hemostatic effect similar to ten units of platelets.[2] The hemostatic efficacy of FWB has been documented in numerous reports describing military, civilian trauma center, and operating room use to treat coagulopathic bleeding.[1,4,8,22–25] In a retrospective study of the results of the FWB procedures for one forward-deployed US military hospital in 2004, 87 patients received 545 units.[26] Fresh whole blood was called for after a patient was identified as requiring a massive transfusion. Transfusion of FWB resulted in significant improvements in both hemoglobin concentration (from 9.0 ± 2.6 to 10.7 ± 1.9 g/dL) and coagulation parameters (international normalized ratio from 2.0 ± 1.1 to 1.6 ± 0.9).

The nature of military medical logistics limits the availability of FFP, platelets, and cryoprecipitate for transfusion in theater, giving the battlefield surgeon few options in the treatment of traumatic coagulopathy. However, the use of FWB in massively transfused patients may circumvent the problem of dilutional coagulopathy. Consider the mixture of one PRBC unit (335 mL) with a hematocrit of 55%, one unit of platelet concentrate (50 mL) with 5.5×10^{10} platelets, and one unit of FFP (275 mL) with 80% coagulation factor activity. This combination results in 660 mL of fluid with a

hematocrit of 29%, 88,000 platelets per microliter, and 65% coagulation factor activity. In contrast, FWB is replete with functional platelets as well as fully functional clotting factors. A 500 mL unit of FWB has a hematocrit of 38 to 50%, 150,000 to 400,000 platelets per microliter, and 100% activity of clotting factors diluted only by the 70 mL of anticoagulant. In addition, the viability and flow characteristics of fresh RBC are better than their stored counterparts that have metabolic depletion and membrane loss.

FWB LOGISTICS

At the earliest level of surgical care in the combat trauma evacuation chain, the Forward Surgical Team (FST), no blood component therapy other than PRBC is doctrinally available. This is because of the resource-intensive nature of the storage of FFP and platelets. The FST is tasked with providing lifesaving surgery, frequently in damage-control scenarios, and typically keeps a limited supply of PRBC on hand, a supply that can be rapidly used up by one severely injured casualty. In combat trauma care, FWB is used in circumstances where bleeding coagulopathic patients require component therapy that is unavailable because of logistical considerations or in situations where RBC requirements have outstripped the available supplies. Although there is no universal, military-wide protocol for the integration of FWB into a resuscitation algorithm, its use has proven invaluable and indeed lifesaving in many situations.

Platelet apheresis is currently being performed at a single site in the combat theater. Although this may reduce the need for FWB, the apheresis system is bulky, resource-intensive, and not suitable for earlier entry levels of care. The materials for the collection and transfusion of FWB are available to medical units through standard military supply channels before deployment. These include phlebotomy kits, collection and transfusion tubing, citrated blood bags, and reagents for blood typing. These items are inexpensive, light, durable, and easy to transport in contrast to the expensive and bulky refrigeration and laboratory equipment necessary for the fractionation and storage of large amounts of traditional blood products. To eliminate the need for blood donor typing in the field, personnel are typed before deploying and a standard pool of blood type-O donors are identified for FWB transfusions. Though any in-theater walking donor program should be instituted with the realization that operational readiness even for young, physically fit military donors may be affected by donation, FWB from walking donors is an especially useful therapy for coagulopathic patients presenting to far-forward deployed FSTs. Most medical units are currently preparing before deployment for the collection and transfusion of FWB in theater.

Blood donation by otherwise fit individuals has been demonstrated to decrease maximal oxygen consumption during exercise, although no impact is seen on submaximal performance.[27] Additionally, removal of approximately 500 mL of whole blood impairs acute cutaneous regulation of body temperature, although this effect is likely related to

Table 2 Combat Casualty Care Recommendations for the Collection, Treatment, and Storage of Fresh Whole Blood

Donation
  Develop a predeployment roster of prescreened donors
    ABO and Rh
    Transmissible diseases
  In emergency situations
    Prefer previous and type O donors
    Perform onsite ABO typing
      Perform direct crossmatch if possible
    2–11% of ID "dog" tag blood types can be incorrect
Treatment
  Use approved blood recipient set (contains anticoagulant)
    Fill until 650-mL bag is nearly full (approx 450 mL blood)
    Draw crossmatch and transmissible disease blood tubes
      Submit to supporting lab even after use of blood
Storage
  Keep fresh warm blood no longer than 24 hours
    If less than 8 hours old, may be refrigerated for 3 weeks

Adapted from Lounsbury DE and Bellamy RF.[30]

acute hypovolemia and altered peripheral vascular tone rather than anemia.[28,29] Although the red cell mass removed during blood donation cannot be rapidly returned, the effect of the loss of the intravascular volume may be offset with an immediate exchange transfusion of a colloid solution such as Hextend. Current combat casualty care recommendations for donation, treatment, and storage procedures for whole blood in theater are listed in Table 2.[30]

WASTAGE

Assuring the availability of conventional PRBC in a combat theater is the duty of the Armed Forces Blood Program and, in OIF specifically, the Southwest Asia Theater Blood Program. To meet this requirement, over 90,000 units of PRBC were sent to Iraq in the first year of the war; about 75,000 units during the first 10 months covered by the review above. Altogether, 1,697 of these units were used to treat US casualties for a usage rate of just over 2%. PRBC wastage rates are high, even for individual actively engaged units such as the 2nd Armored Cavalry Regiment (ACR) and 274th FST, where wastage was reported as 87% and 94%, respectively (personal communication). High rates of RBC wastage have also been noted in the Korea, Vietnam, Bosnia, and Kosovo conflicts. Even though RBC were sent to these theaters in amounts 50 times in excess of use, local shortages occurred because small, mobile surgical units had limited carrying capacity and occasionally high demand.[9] This inefficient use of resources is inevitable on the battlefield because of the episodic nature of combat injury and the necessity of forward-deployed medical units to be prepared at all times to receive casualties. Current military medical doctrine mandates that forward surgical assets including the FSTs, where initial damage-control operations for severe hemorrhage are frequently performed, be issued 10 to 20 units of type-O PRBC at a time.[31,32] Blood resupply is via higher levels of care, which frequently face an increased need for blood products concurrently with the FSTs. ABO-specific PRBC and FFP as well as limited platelet concentrate and cryoprecipitate are available at higher levels of the evacuation chain such as combat support hospitals, where more definitive surgical procedures are undertaken. Further contributing to wastage, units of FFP frozen for transport at very low temperatures routinely break upon thawing, resulting in a 25% to 50% rate of wastage.

FWB SAFETY

All military personnel, and thus the population of potential walking FWB donors, are screened for or immunized against human immunodeficiency virus (HIV), hepatitis B and C, and other common bloodborne pathogens. Bacterial contamination of FWB is a risk under field conditions, but is rare after 8 hours of warm storage in the United States. At the time of collection, all donors undergo standard risk questionnaire screening and are tested for anemia. After each FWB transfusion in theater, samples of both donor and recipient blood are sent to the Armed Forces Blood Program for analysis. The results of this testing have been extensively monitored for rates of infection.[33] Of 2,222 donor samples tested between May 2003 and August 2005, there were three hepatitis C antibody confirmations by recombinant immunoblot assay, one sample indeterminate for HIV, and a single human T-cell lymphocytic virus by Western blot. For blood component therapy in the United States, the risk of infection with either HIV or hepatitis C is one for every two million units.[34] Given that FWB transfusion is currently used as a lifesaving therapy in the face of otherwise untreatable coagulopathy, in the absence of the availability of appropriate blood component therapy, the use of fresh whole blood appears to be safe and beneficial.

CONCLUSION

Fresh whole blood transfusion is extremely rare in civilian trauma centers that have ready access to a robust supply of PRBC and blood products.[1,22,23] Because the majority of transfused civilian trauma patients receive only one to four units of PRBC and no FFP, donated blood supplies can be utilized more efficiently and economically than FWB by fractionating whole blood into its components and transfusing according to patient-specific clinical demands.[35] However, modern combat operations frequently strain medical logistic capabilities, limiting the availability of the modern spectrum blood components required by hemorrhaging, coagulopathic patients.[10,32,35] It is in this context that the lifesaving potential of FWB is most evident. Data from OIF demonstrate that even a small number of severely injured casualties can rapidly use up available supplies.

FWB transfusion in military trauma fills a void left by the unpredictable nature of combat casualty care and military logistics. It is a convenient, safe, and effective treatment for many patients who might otherwise die. Fresh whole blood is best utilized when the demand for blood exceeds supply, or when coagulopathy cannot be treated with available blood products.

The continued use of FWB in combat casualty care is warranted, especially at the level of the FST where the supply of PRBCs is small and component therapy is unavailable. All FST personnel should be trained in rapid blood typing and collection techniques before deployment to combat theaters. FWB transfusion in a combat theater should be part of an integrated approach to preventing and interrupting the vicious cycle of traumatic coagulopathy. Novel hemostatic agents, the prevention and treatment of hypothermia, and effective resuscitation with awareness of the potential for rebleeding with overly aggressive resuscitation should all augment FWB transfusion in modern military trauma care.

ACKNOWLEDGMENTS

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